REMARKS

I. Amendments

By this amendment, claim 1 has been amended to incorporate specific limitations of the dependent claims. The amendment is made without prejudice to the filing of future continuing applications.

This amendment adds no new matter to the specification

No amendment of inventorship is necessitated by this amendment.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version with Markings to Show Changes Made".

II. Traverse of the Rejection under 35 U.S.C. Sec. 102(b) over Stevenson *et al.*

Claim 1 as now amended is not anticipated by the teaching of Stevenson *et al.* (The Diabetes Manual, 1995 article).

Stevenson *et al.* do not teach treatment of Tumor Necrosis Factor-alpha mediated diabetic complications selected from the group consisting of retinopathy, nephropathy, neuropathy and disorders of the arteries in a mammal. Nor does the cited reference teach administration of a dose of 0.1 mg/kg to 30 mg/kg to a mammal.

Stevenson *et al.* fail to teach each and every limitation of the claimed invention, the Sec. 102(b) rejection over Stevenson *et al.* must be withdrawn.

III. Traverse of the Rejection under 35 U.S.C. Sec. 102(b) over Szalkowski *et al.*

Claim 1 as now amended (and dependent claims thereon) are not anticipated by Szalkowski *et al.* (Endocrinology, 1995 article).

Szalkowski *et al.* do not teach treatment of Tumor Necrosis Factor-alpha mediated diabetic complications selected from the group consisting of retinopathy, nephropathy, neuropathy and disorders of the arteries in a mammal. Nor does the cited reference teach administration of a dose of 0.1 mg/kg to 30 mg/kg to a mammal.

Szalkowski *et al.* does not teach each and every limitation of the claimed invention the Sec. 102(b) rejection over Szalkowski *et al.* must be withdrawn.

IV. Traverse of the Rejection under 35 U.S.C. Sec. 103 (a) over Stevenson *et al.* and Szalkowski *et al.* and under 35 U.S.C. Sec. 103 (a) over Ikeda *et al.* and Stevenson *et al.*

Claims 10 and 13 have been rejected under 35 U.S.C. Sec. 103(a) as being unpatentable over Stevenson *et al.* (The Diabetes Manual, 1995 article) and Szalkowski *et al.* (Endocrinology, 1995 article).

Applicant's object to the Examiner's improper characterization of the disclosure and *ad hoc adjudication* misrepresenting the Applicant's position as made on page 8, line 7:

"Moreover, according to Applicant's admission regarding the prior art ...."

and on page 10, lines 4-7:

"Applicant's admission regarding the prior art ...."

and on page 10, last line summarizing the rejection:

"...based on Stevenson et al. and Applicant's admission herein."

The Applicants have made no admission as to the prior art. Since the Examiner does not even bother to specifically point out where in the specification he has discovered these "admissions", the applicant is fully prejudiced and deprived of any ability to traverse and rebut this summary rejection with particularity. On this basis alone, the rejection must be withdrawn.

The disclosure clearly describes that the cited disease states are the types of inflammation that can be treated by the methods of the claimed invention. There is no admission as to what is or is not prior art. Since the Examiner does not even bother to specifically point out where in the specification he has discovered these "admissions", the applicant is deprived of any ability to traverse and rebut the rejection without prejudicing his own arguments.

By these statements and reliance upon *ad hoc adjudication*, the Examiner's own words demonstrate that the rejection is improperly based upon a characterization of the prior art that is founded upon the Examiner's personal opinion and **not** on the evidence of record. The Examiner has failed to make a proper *prima facie case*.

As previously argued, neither combination of asserted references, alone or in combination teach or suggest therapeutic treatment of TNF-α mediated inflammatory disease. The Examiner admits that none of the asserted art teach treatment of TNF-alpha mediated inflammation. (Page 7, 1st paragraph, and Page 9, 4th paragraph). The asserted combination of art does not teach or suggest the claimed invention, or provide any reasonable expectation for success. It is improper to assert personal opinion as a substitute for the lack of required motivation or teaching in the asserted prior art. This rejection is based upon the improper use of hindsight.

Claim 1 as amended, without prejudice, is clearly free from the asserted combination of art. It is clear that the art does not teach treatment of Tumor Necrosis Factor-alpha mediated diabetic complications selected from the group consisting of retinopathy, nephropathy, neuropathy and disorders of the arteries in a mammal by the administration of a dose of 0.1 mg/kg to 30 mg/kg to a mammal.

The Examiner admits that none of the asserted art teach treatment of TNF-alpha mediated inflammation. (Page 7, 1st paragraph, and Page 9, 4th paragraph). There is no evidence on record to support maintaining this rejection.

Applicants respectfully request withdrawal of the Sec. 103(a) rejection over Stevenson *et al.* and Szalkowski *et al.* and rejection over Ikeda *et al.* and Stevenson *et al.*

V. Traverse of the Double Patenting Rejection

Claims 1-12 have been rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,965,584 in view of Stevenson *et al.*

The cited claims are directed to methods for treating diabetes, the present claims are directed to methods of treating specific TNF-alpha mediated complications.

Therefore, Applicants respectfully request withdrawal of the judicially-created obviousness-type double patenting rejection.

VI. Conclusion

Reconsideration and allowance of the claims as amended is requested. Applicants request that the holding of finality be withdrawn and an additional opportunity to respond be granted should the amendment and traverse fail to overcome the Examiner's rejection.

Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, the Examiner is respectfully requested to call Applicants' attorney at the number below.

Should the amendment and traverse be deemed not to overcome all remaining rejections, entry of the amendment for purpose of appeal is requested.

Respectfully submitted,

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